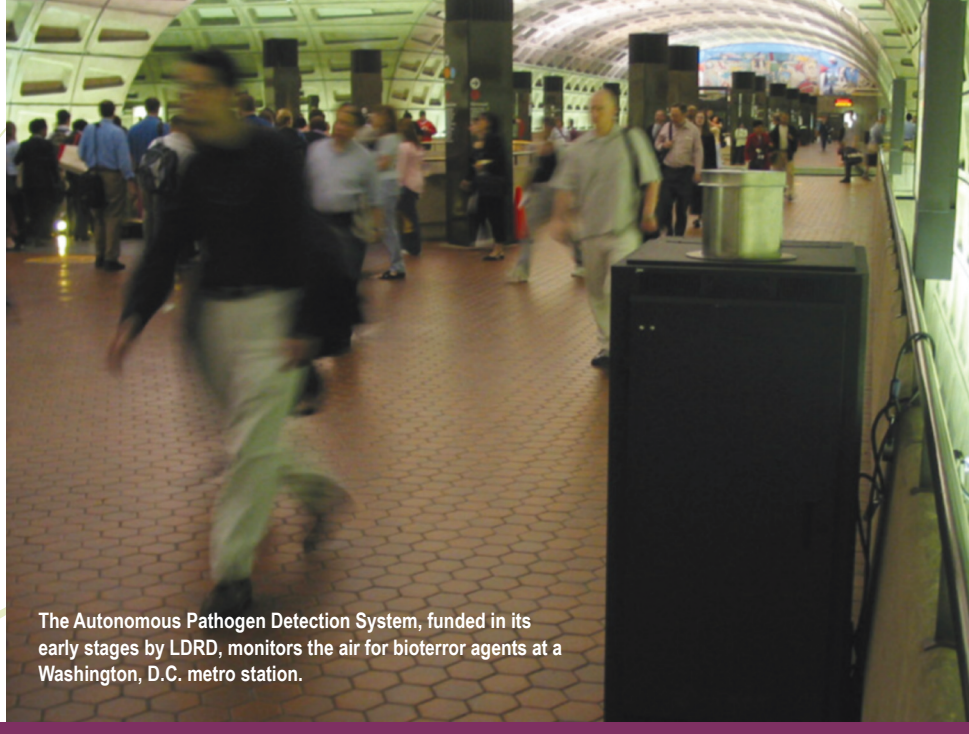
An LDRD Success Story

University of California
Lawrence Livermore National Laboratory



The Autonomous Pathogen Detection System, funded in its early stages by LDRD, monitors the air for bioterror agents at a Washington, D.C. metro station.

Countering Bioterrorism

Thanks to Laboratory Directed Research and Development (LDRD) funded research, Lawrence Livermore has developed several field detectors to provide rapid, accurate, and sensitive early-warning systems for biological attacks. Early detection is key to saving lives and preventing the spread of disease.

Getting Results Fast

Previously, bioagent identification could only be done in a laboratory and took days to weeks. However, Livermore technology advances led fully automated biodetectors for real-time sample collection, detection, and identification in the field.

The Autonomous Pathogen Detection System (APDS)—one such detector developed at Livermore—monitors the air continuously and uses advanced technologies to reduce false alarms. It can measure up to 100 different agents per sample and reports identified agents within an hour. About the size of a corner mailbox, the APDS could be placed in a large area such as an airport or a stadium. The system also can be adapted for situations where environmental or clinical pathogens require monitoring. For example, APDS could test for mold or fungal spores in buildings or for the airborne spread of contagious materials in hospitals. It also could identify disease outbreaks in livestock transport centers or feedlots.

An Early-Warning System for Biological Attacks

Development of the Autonomous Pathogen Detection System

- In 1995, although bioterrorism seems a remote possibility to most, the Laboratory decides to invest in research to address a threat for which there is little technological answer. LDRD helps fund a program to counter biological attacks with early-warning systems.
- In 1996, the project that would lead to the Autonomous Pathogen Detection System (APDS) is funded by DOE as a major project in the new Chemical and Biological Nonproliferation Program.
- By late 1998, two types of automated biodetectors for real-time biothreat identification are fielded: a miniature flow cytometer that looks at the proteins and other material on the surface of cells, and a portable PCR (polymerase chain reaction) unit, the Advanced Nucleic Acid Analyzer (ANAA), that identifies DNA inside the cell. These set the stage for APDS.
- In 2000, an APDS prototype is fielded for a 12-hour test.
- By 2002, Livermore is testing the second APDS unit that runs multiplexed assays unattended for at least a week at a time, with results transmitted via a radio contact.
- In September 2003, the APDS passes exposure tests for two live bioagents—anthrax and plague—at a high-containment laboratory at the Dugway Proving Ground in Utah. The APDS project is also transitioned from DOE to the new Department of Homeland Security.
- In 2004, the APDS is ready for deployment. The development team is honored with a 2004 R&D 100 Award, and the system is featured on the cover of *Analytical Chemistry*, showing it in place at a Washington, D.C. metro station.
- Because of advances such as APDS, Lawrence Livermore is a leader in the fight against biological terrorism, and is a major participant in the DHS multi-laboratory Chemical and Biological Countermeasures Program.

About LDRD

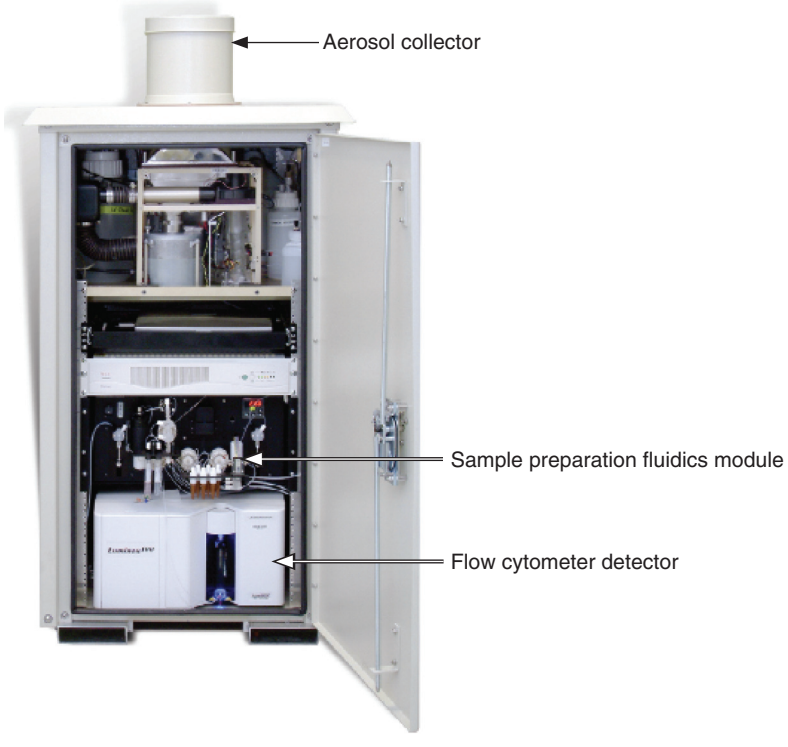
The Laboratory Directed Research and Development (LDRD) Program is LLNL's primary mechanism for funding cutting-edge R&D to enhance the Laboratory's scientific vitality. Established by Congress in 1991, LDRD collects funds from sponsored research and competitively awards those funds to high-risk, potentially high-payoff projects aligned with Laboratory missions.

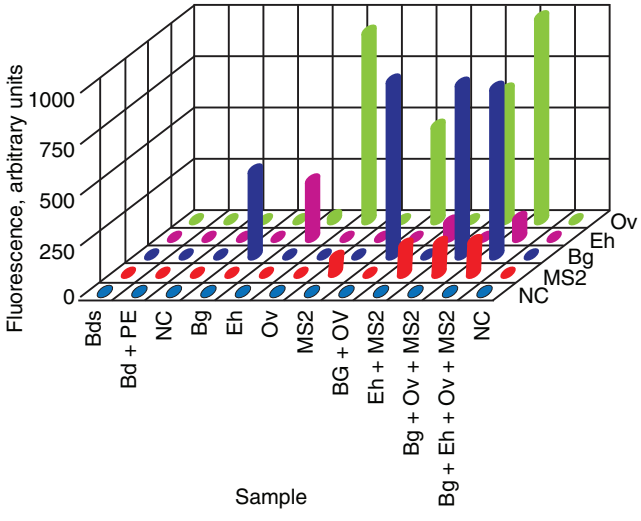
The team responsible for developing the Autonomous Pathogen Detection System combines Livermore Laboratory expertise in biological science, engineering, microtechnology, computer modeling, systems analysis, and atmospheric science.

How the APDS Works

After APDS collects air samples and suspends them in aqueous solution, it tests them with PCR (DNA-based) assays. The immunoassay detector incorporates liquid arrays, a multiplexed assay that uses polystyrene microbeads coated with thousands of antibodies and colored with a unique combination of red- and orange-emitting dyes. When the sample is exposed to the beads, a bioagent, if present, binds to the bead with the appropriate antibody. A second fluorescently labeled antibody is then added to the sample, resulting in a highly fluorescent target for flow analysis. System software compares the result with preset threshold criteria for a positive identification.

The newest version of APDS also runs a genetic test using multiplexed PCR. For this test, the sample is first mixed with reagents capable of identifying all target organisms, then introduced into the PCR system, a Livermore-designed thermal cycler mounted in line with the sample-preparation unit. After specific nucleic-acid signatures associated with the target bioagent are amplified up to a billion-fold in the reaction, the reaction products are analyzed on the same multiplexed identifier used for the immunoassay. Results are transmitted every 2 hours to a control center, where the instrument's performance is monitored. The system can run unattended for 1 week.





Biological Targets

Bg = Bacillus globigii simulates anthrax (bacterial spore)
Eh = Erwinia herbicola simulates plague (vegetative bacteria)
MS2 = Bacteriophage MS2 simulates smallpox (virus)
Ov = Ovalbumin simulates Botulinum toxins (protein)
AC = Antibody control

Control Beads

Bds = Beads alone
Bd + PE = Phycoerythrin (fluorescent reagent)
NC = Negative control
FC = Fluorescent control
AC = Antibody control

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